no teaching which would suggest the presently claimed ultrafine L-carnitine, or the various claimed compositions and methods. Accordingly, these references cannot affect the patentability of the present claims.

The rejection of Claims 1-14 under 35 U.S.C. § 103(a) in view of U.S. Patent No. 4,602,039 (Cavazza I) in view of U.S. Patent No. 6,063,820 (Cavazza II) is respectfully traversed.

Cavazza I is discussed on page 5, lines 14-22, of the specification. Thus, as explained in the specification, the undisputed difference between the L-carnitine of Cavazza I and the presently claimed ultrafine L-carnitine is that the presently claimed ultrafine L-carnitine and salts thereof have a particle sufficiently small that substantially all of it passes through a 100, or even a 150 or 200, United States Bureau of Standards (USBS) mesh screen. In contrast, the L-carnitine and salts thereof prepared by the methods described in Cavazza I have a particle size such that more than 10% by weight of the L-carnitine is retained by a 50 mesh sieve and more than 40% by weight is retained by a 100 mesh sieve. Furthermore, not only is this deficiency in the Cavazza references undisputed, the Examiner has explicitly recognized this deficiency stating: "The Examiner notes that that cited references do not teach the claimed particle sieve size" (paper number 5, page 3, lines 7-8).

Despite the numerous and distinct advantages proffered by the presently claimed ultrafine L-carnitine, which Applicant submits could not have been expected based on the teachings of the cited references (see Amendment and Request for Reconsideration filed on November 4, 2002, as well as pages 1-5 of the present specification), the Examiner chooses to dismiss these advantages and question the criticality of the claimed specific particle sieve size. To address the Examiner's assertions and questions, Applicant now submits the attached, executed Declaration under 37 C.F.R. §1.132 by Mr. Raj K. Chopra (hereinafter referred to as the "Chopra Declaration").

As demonstrated in the Chopra Declaration and the attached Exhibit A, Mr. Raj K. Chopra is currently the President and Chief Scientific Officer of Tishcon Corporation (Westbury, NY) and has 34 years of experience in the Nutritional Supplement Industry. In addition to numerous scientific presentations and publications, Mr. Chopra has accumulated an expertise in the areas of: a) formulation of solid, semisolid and liquid dosage forms; b) taste and flavor masking of micro and macronutrients; c) enhancing dissolution and bioavailability of nutrients; and d) formulating test supplements for clinical trials. Equally importantly, Mr. Chopra is a significant user of ultrafine L-carnitine and is very familiar with its properties and uses.

After reviewing Cavazza I, Cavazza II, the specification and claims of the above-identified application, and the June 4, 2002 Office Action, Mr. Chopra has provided the attached Chopra Declaration highlighting the fact that "the ultrafine L-carnitine described and claimed in the present application exhibits a number of unexpected advantages as compared to the L-carnitine described in Cavazza" (see numbered paragraph 9). Applicant notes that the claims have not been amended in response to the June 4, 2002 Office Action and the obviousness rejection over Cavazza I in view of Cavazza II has been maintained and reissued in the November 29, 2002 Office Action. Accordingly, the Chopra Declaration is appropriate and applicable to address the current rejection explicated in the November 29, 2002 Office Action.

As stated in the Chopra Declaration, Mr. Chopra's opinion is based on experience and use of both the ultrafine L-carnitine described and claimed in the present application and the conventional L-carnitine described in Cavazza (see paragraph 11 of the Chopra Declaration). Specifically, Mr. Chopra has used both conventional L-carnitine and ultrafine L-carnitine provided by Sigma-Tau Healthsciences in the formulation of dietary supplement dosage forms (soft gelatin capsules, hard gelatin capsules, and tablets) at Tishcon Corporation and

have found that the ultrafine L-carnitine provides the following unexpectedly superior results:

A. The particle size reduction achieved with the claimed ultrafine L-carnitine has enabled Tishcon Corporation to design a soft-gel dosage form of ultrafine L-carnitine (for example fumarate) in combination with 1) omega-3 fatty acids in fish oil; 2) coenzyme Q10; and 3) alpha lipoic acid. The same good results have not been obtained using L-carnitine produced according to Cavazza I (see paragraph 12 of the Chopra Declaration).

B. The fineness of the particle size, as well as the particle size range of the claimed ultrafine L-carnitine, provides an ideal physical form to ensure content uniformity when filling multi-component active products in two piece hard gelatin capsules. Furthermore, Tishcon Corporation has been able to obtain a high degree of color uniformity in its tablets made with the claimed ultrafine L-carnitine. Particularly, in the soft gelatin encapsulation process, where the L-carnitine (for example fumarate) is processed into a paste with added vegetable oils, the particle size is a critical factor. The claimed ultrafine L-carnitine performs perfectly in this process, while the conventional L-carnitine (for example fumarate) with its larger particle size range causes severe filling as well as sealing problems (see paragraph 13 of the Chopra Declaration).

C. Due to the extremely fine state of subdivision afforded by the presently claimed ultrafine L-carnative, Tishcon Corporation is able to pack the powder more firmly in capsules, thereby leaving very little interstitial spaces between particles. This is probably the reason why these capsules do not exhibit premature:

1. discoloration;

2. development of unacceptable odor;

3. moisture pick-up; and

4. physico-chemical instability (see paragraph 14 of the Chopra Declaration).

Mr. Chopra also states that the ultra-fine L-carnitine and salts thereof of the present invention has a particle sufficiently small that substantially all of it passes through a 100, 150, or 200 United State [*sic*, States] Bureau of Standards (USBS) mesh screen, while L-carnitine and salts thereof prepared by the methods described in Cavazza I have size of such that greater than 10% by weight of the L-carnitine is retained by a 50 mesh sieve and more than 40% by weight is retained by a 100 mesh sieve (see paragraph 11 of the Chopra Declaration). Moreover, Mr. Chopra states that these results would not be expected based on the disclosure of Cavazza I (see paragraph 11 of the Chopra Declaration).

Thus, at the time the present invention was made there was a need for preparing compositions containing L-carnitine and one or more other ingredients with which bulk L-carnitine is not miscible, (*e.g.*, oil-based raw materials). Moreover, at the time the present invention was made there was also a need for reducing the hygroscopicity of L-carnitine.

In other words, even though the L-carnitine (for example the fumarate salt) prepared according to Cavazza I demonstrates an improvement in handling abilities, for example for tabletting, over previous forms of carnitine, the L-carnitine prepared according to Cavazza I still possesses a particle size and bulk density that is less than ideal for certain other applications, such as containment within hard and soft geltain capsules (see paragraph 10 of the Chopra Declaration). For this reason, many transformers rejected its use for hard and soft gel applications, choosing to remain with tablets.

It was not obvious to reduce the size of the particles as disclosed in the present application, since this was felt unworkable (see paragraph 10 of the Chopra Declaration). Specifically, carnitine in any form is seldom a candidate for particle size reduction, because

the frictional heat generated during the particle size reduction process may induce the humid state relative to the ambient air temperature and thereby produce sticking (see paragraph 10 of the Chopra Declaration).

For the reasons set forth above and in the Chopra Declaration, the presently claimed ultrafine L-carnitine is not obvious in light of Cavazza I and the claimed particle sieve size is, in fact, a critical parameter, which provides *unexpectedly superior* results.

Applicant submits that Cavazza II cannot cure the basic deficiencies of Cavazza I for the following reasons. Cavazza II discloses carnitine and salts thereof in combination with other active ingredients. However, the L-carnitine used in Cavazza II is produced using the method described in Cavazza I and, thus, has the characteristics of that of Cavazza I.

However, as explained above, only by using ultrafine L-carnitine in combination with omega-3 fatty acids in fish oil or coenzyme Q10, or alpha lipoic acid, is it possible to obtain an easily workable mixture. The same good results would not have been obtained using L-carnitine produced according to Cavazza I.

Moreover, Cavazza II does not mention or suggest the use of the ultrafine L-carnitine according to the present claims. For these reasons Cavazza II alone, or even in combination with Cavazza I, can not render the present invention obvious.

Based on the foregoing, supported by the Chopra Declaration, Applicants submit that the presently claimed ultrafine L-carnitine is not obvious in view of the combined disclosures of Cavazza I and Cavazza II. In particular, the claimed particle sieve size is, in fact, a critical parameter, which provides *unexpectedly superior* results. Accordingly, the rejection should be withdrawn.

Applicants submit that the application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

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